Born for a Noble Cause? -- -*A case study on Fanconi Anemia*

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Abstract: The fictional case study presented here is not based on one case, but is actually based on several cases. College students enrolled in a bioethics course for non-majors wrote it. The case entails the thought processes and decision-making involved in order to save one child suffering from a genetic disorder by producing another child, a "designer baby." Nursing majors from a freshmen level college General Biology course participated in the suggested activities.

Keywords: Fanconi Anemia, bioethics, in-vitro fertilization, preimplantation genetic diagnosis

MY STORY

The day I was born I had the potential to save my brother's life. My name is Gene. I am a designer baby. I was designed, created, and born for the specific purpose of saving his life. My brother was diagnosed with Fanconi Anemia (FA), an illness that is fatal unless a successful bone marrow transplant can be performed. My parents first thought was that they would be more than happy to donate marrow to their child, but neither of them was a match nor was any other member of their extended family. It was around this time that their doctor suggested having another child who could be a donor. Having a basic knowledge of biology, my parents knew that the odds of a new child being a match was 25% along with a 25% chance of the new child also having Fanconi Anemia. These did not seem like very good odds to them, so they sought out a doctor who could ensure that the new baby would be a genetic match and would not have the disease. This doctor was a specialist in the area of *in-vitro* fertilization (IVF) and preimplantation genetic diagnosis (PGD). IVF is the creation of an embryo in a lab using donated sperm and eggs. PGD is the testing of early embryos for specific traits prior to implantation inside the mother. This process allows parents to create babies screened for specific traits. In my specific case, my parents designed me to be a match for my brother and to not possess the gene for FA. This would guarantee that I would be born healthy and that I would be a genetic match for my brother so that I could donate bone marrow which could be used to save his life.

Now that my parents knew they could create a child to save the one they already had, they had to decide if they should and also if they would. They were in an extremely emotional state at the time. They had to deal with this decision, while also coping with my brother's illness. They were under an extreme amount of stress at the time and facing a very difficult decision. They had to consider whether or not it was right to create a new child to save their firstborn. They had to face the prospect of raising another child, paying for the expensive procedure to create him, and of the reaction of their friends and families regarding whatever decision they made. It was a very difficult decision for them. They agonized over it. They consulted with doctors, lawyers, clergy, friends, and family. After learning all that they could and weighing the consequences of either decision they made the only decision they really could, to save the life of their child.

This is where I come in. Having decided that they wanted to go ahead with having me, they needed to design me. They wanted to ensure that I would be a match for my brother and that I would not have FA. They accomplished both of these goals through the use of PGD. The embryo that would

eventually become me was implanted into my mother and nine months later I was born. After my birth, bone marrow was harvested from my hip. This bone marrow was transplanted into my brother. This healthy bone marrow would hopefully cure his FA.

THE TECHNOLOGY BEHIND THE STORY

In-vitro fertilization is accomplished through a simple yet costly procedure. The average cost for a procedure to be completed is approximately $12,400 in the United States (WebMD Health, 2003). First, the woman is sedated to avoid discomfort and pain. Then, using the ultrasound-guided-trans-vaginal method, eggs are retrieved through a needle, which is inserted through the vaginal wall into the ovaries (Cooper Center, 2004). From there, the retrieved eggs are immediately examined by an embryologist under a microscope. Retrieved egg(s) are then placed into an incubator to allow the eggs to mature. The male donor is asked to donate his sperm to fertilize the egg. The egg(s) and sperm are then combined in a special culture fluid in an incubator and observed. The observation typically lasts approximately eighteen hours after insemination and the beginning stages of development. Once the egg is fertilized, it can undergo PGD, and then be placed in the uterus of the woman. Hormones are given to the mother to sustain the pregnancy (University of Texas, 1997). The pregnancy is then followed through to term. Figure 1 indicates the milestones required for the necessary procedures to produce a designer baby.

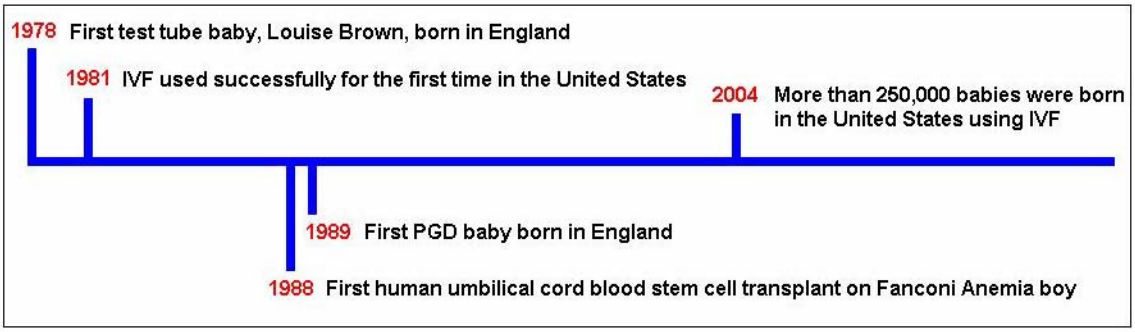

Figure 1. *A timeline of developments in reproductive technology.*

As mentioned, PGD can be used to screen an embryo that will be genetically, a compatible match for his or her sibling. PGD is an expensive procedure, $4,500 dollars to $5,500 dollars, and that is in addition to the cost of IVF. PGD genetically tests embryos to see if they have chromosomal defects, abnormalities, genetic diseases and/or a certain compatibility (PGD: Reproductive Specialty Center, 2004). The test is done three days after IVF takes place, when the fertilized egg has divided into eight cells (Center for Genetics, 2004). These eight cells contain all the same genetic information specific to that individual; therefore, to test the potential child for genetic diseases, a doctor has to remove one of the eight cells and analyze it (The Infertility Center, 2004). After the cells have been screened, the embryos that contain genetic diseases and/or do not genetically match the needs of their sibling will either be discarded or frozen. The embryos that do meet all the criteria will then be implanted into the mother's uterus (Figure 2). They will hopefully attach to the uterine wall, develop for nine months, and be delivered as a full term normal baby (Monash, 2004).

What is Fanconi Anemia (FA)?

Fanconi anemia (FA) was first described by a Swiss pediatrician, Guido Fanconi. In 1927, Dr. Fanconi published his clinical observations on brothers who had inherited several abnormal physical conditions and who also experienced bone marrow failure. These children suffered severe life-threatening aplastic anemia. Their blood systems could not successfully combat infection. In addition, as a result of anemia, they were chronically fatigued. Because their platelet counts were low, they suffered spontaneous bleeding. Thus, when research was conducted it was found out that Fanconi anemia is an "inherited" anemia. It is one of several rare genetic conditions that lead to aplastic anemia. No one has yet explained why FA patients develop bone marrow failure. Understanding can come only after the FA genes have been isolated and studied. However, scientific studies show that almost all FA patients will eventually experience marrow failure. Some scientists believe that the interaction between toxic environmental factors and an FA patient's genetic vulnerability to marrow failure may contribute to aplastic anemia (Fanconi Anemia, 2004). Individuals with Fanconi Anemia should avoid x-rays, chemotherapeutic agents, and other environmental exposures. Other symptoms include severe aplastic anemia, hypoplasia of the bone marrow and patchy discoloration of the skin. Thus, treatment usually consists of bone marrow transplant.

Fanconi anemia is a recessive disorder. Both parents must be carriers of a recessive FA gene for their child to be born with this disorder. If both parents carry the recessive gene, the chances are one in four that any of their children will inherit the disease. Scientists call this pattern of inheritance autosomal recessive (Figure 3).

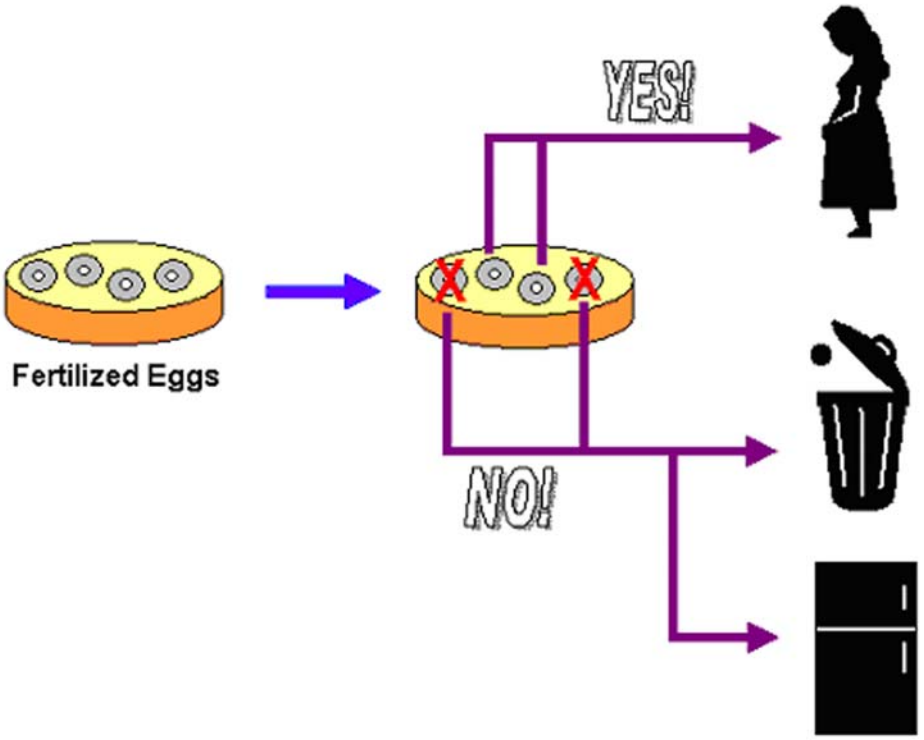

Figure 2. *Fertilized eggs are screened for genetic defects and compatibility. The eggs that are defect free and genetic matches are implanted into the mother's uterus. The eggs that are incompatible or contain genetic defects (labeled X) are either frozen or discarded. Graphics created by Gloria Lu.*

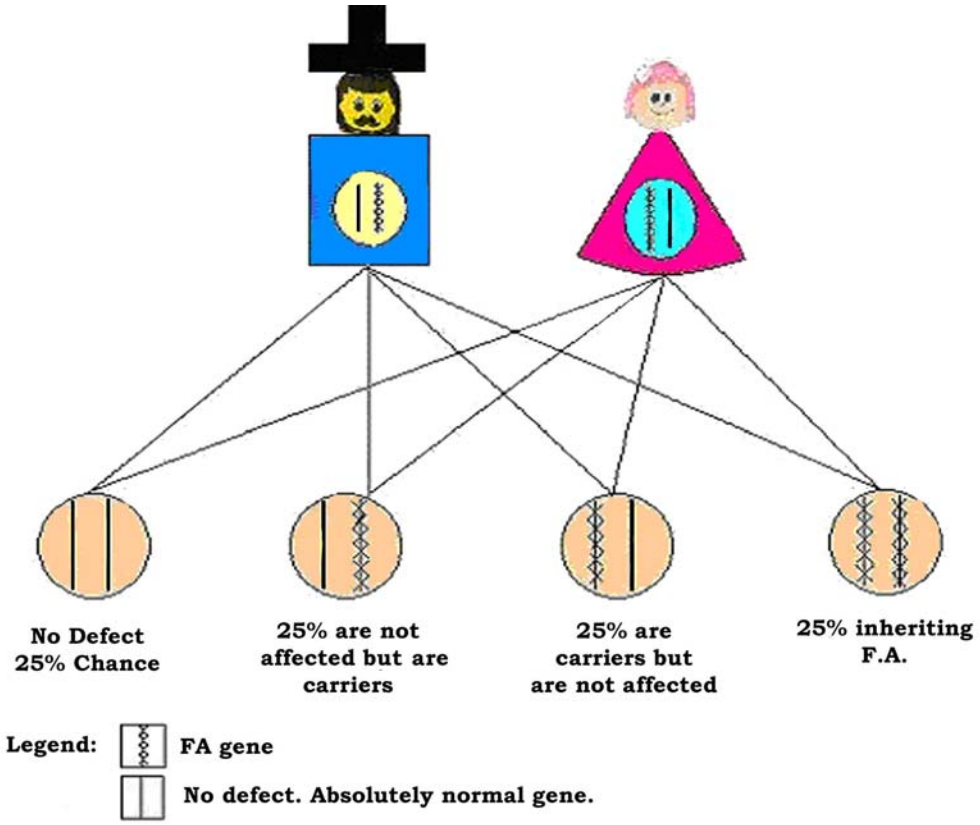

Figure 3. *Above represents the probability of inheriting the Fanconi Anemia if both parents are carriers for the FA gene. The disease spreads if both parents pass the defective gene onto their offspring. Graphics created by Hira Shafqat*

DIAGNOSIS

FA usually reveals itself before children are 12 years old, but, in some very rare cases, no symptoms are present until adulthood. FA patients are usually smaller than average. They may feel extreme fatigue and have frequent infections. Nosebleeds or easy bruising may be a first sign of the disease. Blood tests may reveal a low white blood cell, red blood cell or platelet count or other abnormalities. Sometimes Myelodysplasia (a rare blood disorder that is associated with dysfunctional bone marrow, resulting in a failure of production of red blood cells, white blood cells and platelets.), acute myelogenous leukemia (which is a cancer of the myeloid line of white blood cells (Free Definition, 2004), or squamous cell carcinoma (a type of cancer usually developed in the epithelial layer of the skin and sometimes in different mucous membranes of the body) are some of the diseases that result through FA. Some of most common defects are listed in Table 1.

While the total number of FA patients is not documented, scientists estimate that the number of people carrying a defective gene is between 1 in 100 and 1 in 600 (Fanconi Anemia, 2004).

Table 1. *Physical defects associated with Fanconi Anemia*

- Hand and arm anomalies: misshapen, missing or extra thumbs or an incompletely developed or missing radius (one of the arm bones).
- Skeletal anomalies of the hips, spine, or ribs.
- Kidney problems, including missing or horseshoe kidney.
- Skin discoloration (café-au-lait spots); portions of the body may have a suntanned look.
- Small head or eyes.
- Mental retardation or learning disabilities.
- Low birth weight.
- Gastrointestinal difficulties.
- Small reproductive organs in males.
- Defects in tissues separating chambers of the heart.

PROGNOSIS AND TREATMENT

The reported survival time of patients with Fanconi anemia is highly varied, ranging from 2 to 25 years. Frequent screenings can ensure early diagnosis of the cancers associated with Fanconi anemia. Individuals with Fanconi anemia may wish to store their own bone marrow in case a later treatment diminishes their existing bone marrow. Bone marrow is a spongy tissue found inside bones. The bone marrow in the breastbone, skull, hips, ribs and spine contains stem cells that produce the body's blood cells (red blood cells, platelets, and white blood cells). If a patient develops a disease of the blood cells he or she may require high doses of chemotherapy to destroy the cancer. However, this also destroys normal blood cells. In these cases, transplantation of healthy bone marrow may save a patient's life. Transplanted bone marrow will restore production of white blood cells, red blood cells, and platelets. The healthy bone marrow may be taken from the patient prior to chemotherapy or radiation treatment, or it may be taken from a donor (Bone Marrow Transplant, 2004). This is why Gene was created to donate bone marrow to his brother and save his life from the deadly disease.

THE REST OF THE STORY

I do not have the gene for FA and am a normal, healthy child. I have always been glad that my very existence could save the life of my brother. We have been closer than most siblings and have shared a special bond. I have had no ill physical effects from the procedure and I will be eternally grateful that I could save my brother. However, I will still have questions about the way and reason I was created. Although I love my brother, I have always had feelings of inferiority in regards to our relationship. I have always felt as if he were more important than me due to the lengths that my parents went to save him. My existence is merely a side effect of his treatment for an illness. So even though it may be true that many younger children feel inferior with no real reason, I think that I have a legitimate reason to feel inferior. I will have to live with the knowledge that I was not wanted for my own sake, but for the benefit of my older brother. So while I am a relatively normal child physically, I do have to live my life with my own, very unique emotional burdens.

Suggested Activities:

Activity 1

Divide the class into four groups. Each group should conduct a survey targeting a different group

(i.e. boys vs. girls, athletes vs. non athletes, children vs. adults). The groups should decide which questions they believe are relevant.

In our own survey we asked university students the following three questions, which we felt were relevant. Are you in favor of genetic testing on embryos (figures 4a and 4b)? Are you in favor of creating and testing an embryo in order to save an older sibling (figures 5a and 5b)? Are you in favor of destroying the embryos that do not match (figures 6a and 6b)?

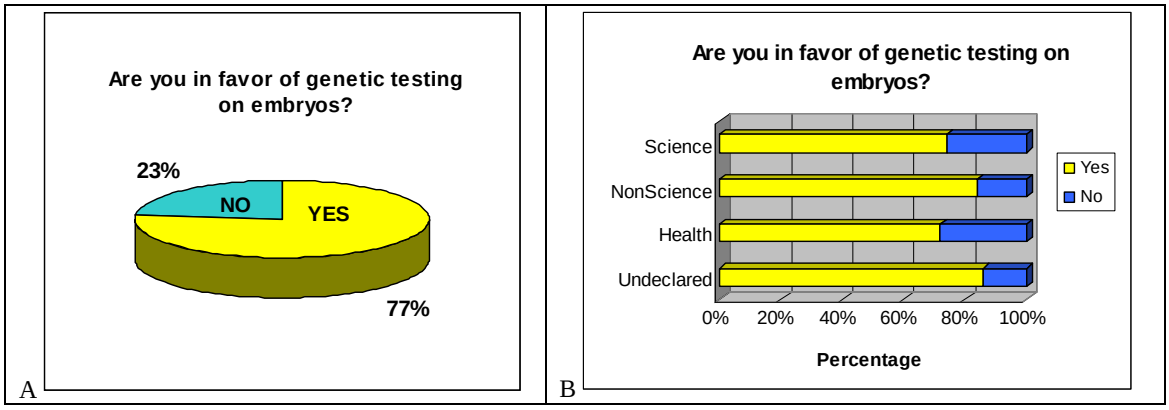

Figure 4. *Results of survey. A). Response of university students(n = 81) when surveyed concerning the question, "Are you in favor of genetic testing on embryos?" B} University students' response based on their background in the health and science fields.*

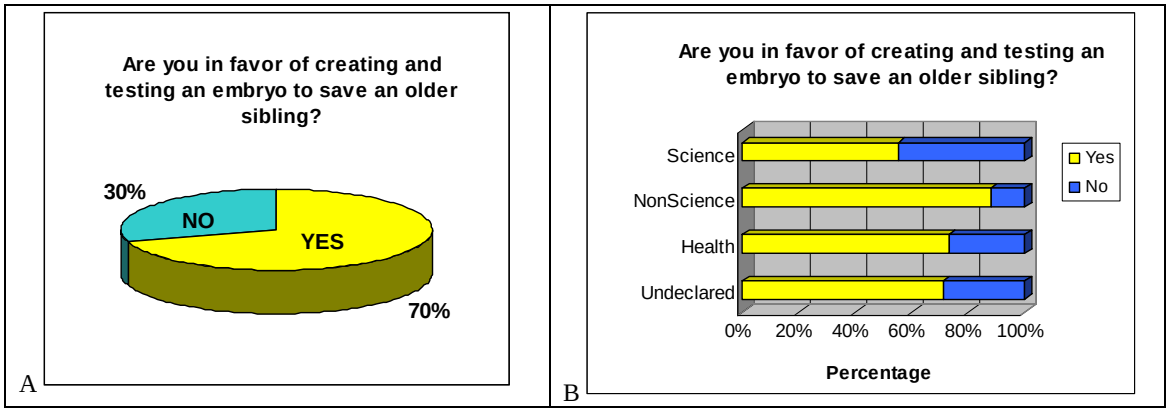

Figure 5. *A) Response of surveyed university students (n = 81) when surveyed concerning the question "Are you in favor of creating and testing an embryo to save an older sibling?" B) Response of university students by background in the health and science fields.*

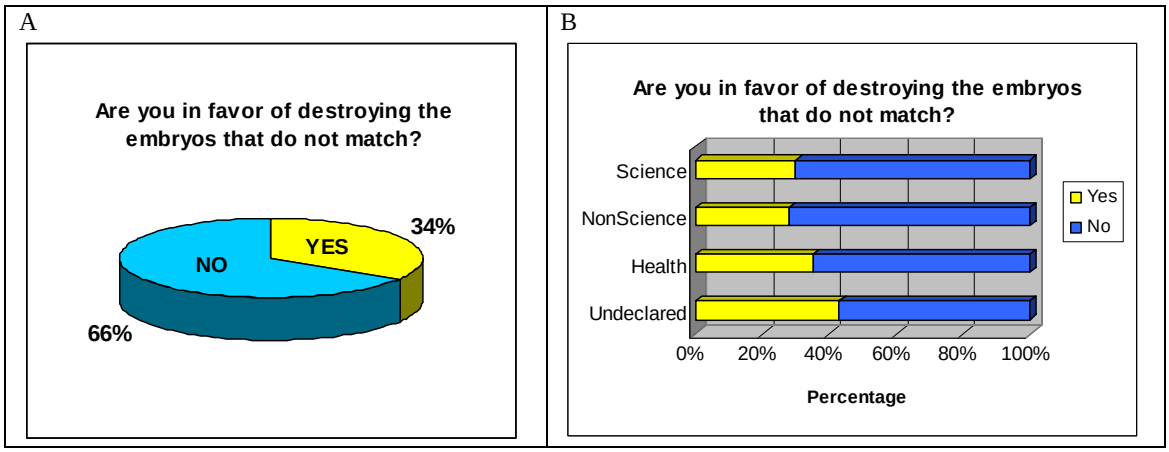

Figure 6. *A) Response of university students surveyed (81) concerning the question, "Are you in favor of destroying the embryos that do not match?" B) Response of university students by background in health or science fields.*

Activity 2

Divide the class into four groups for discussion. Each group will represent an individual interested in the issue of designer babies. Assign one of the following roles to each group: designer baby, sick older sibling, parents, or doctors/genetic counselors. Instruct the groups that they should approach the discussion from the perspective of the role assigned to them. Use the following questions as necessary to guide the discussion or formulate your own questions.

1. Why or why not would a couple with a child who had a fatal genetic illness use IVF or PGD?
2. From your assigned perspective how would you convince someone that IVF and PGD technology should or should not be used?
3. From your assigned perspective what are the advantages or disadvantages of creating a baby to cure a sick older sibling?
4. From your assigned perspective what are the ethical concerns with the use of IVF and PGD technology?

Activity 3

Divide the class into groups of four or five students. Allow each group to do outside research on the topics of IVF, PGD, and genetic engineering (see Table 2 for possible sources). Assign each group a pro or con position on one of the topics. The pro and con groups should debate the topic for five to fifteen minutes, with the rest of the class serving as evaluators and asking questions when necessary. At the end of the debate the rest of the class should assess the arguments made. Figure 7 provides a possible rubric.

Table 2*. Additional sources of information.*

Websites for Additional Research

Most comprehensive website on Designer Babies with additional links
http://www.tecsoc.org/biotech/focusbabies.htm

Good commentary UK Guardian on Baby Nash
http://www.guardian.co.uk/Archive/Article/0,4273,4072039,00.html

Washington Post on Baby Nash
http://www.washingtonpost.com/ac2/wp-dyn/A62318-2000Oct2

Cnn.com on Baby Nash
http://archives.cnn.com/2000/HEALTH/10/03/testube.brother/index.html

This article contains interesting arguments for and against designer babies
http://news.bbc.co.uk/1/hi/health/955644.stm

Website about IVF and Embryo selection
http://dir.salon.com/health/feature/2000/08/21/stem_cell/index.html

Two good articles on IVF and PGD in the UK
http://observer.guardian.co.uk/uk_news/story/0,6903,656109,00.html
http://www.guardian.co.uk/genes/article/0,2763,1266401,00.html

Recent and general article on 'Savior Siblings"
http://www.newscientist.com/news/news.jsp?id=ns99994965

Arguments against Human Embryonic Stem Cell research- contains alot of facts.
http://www.stemcellresearch.org/statement/statement.htm

Stem cell research explained
http://www.guardian.co.uk/genes/article/0,2763,535023,00.html

Comprehensive website about fanconi-anemia, with links
http://www.cancerindex.org/ccw/fanconi.htm#fa2

Henry - A boy living with Fanconi anemia, includes pictures
http://www.hsg.org/

User-friendly website on Bone Marrow Transplants with links
http://www.cancerindex.org/ccw/guide2bm.htm

Class Debate Evaluation

CATEGORY	POINT	TOTAL
Understanding of Topic		
-Team clearly understood topic and presented their information convincingly.	**5 points**	
-Team clearly understood topic and presented their information with ease.	**4 points**	
-The team seemed to understand the main points and presented those points with ease.	**3 points**	
-The team did not show an adequate understanding of the topic.	**2 points**	_____
-All information presented was accurate, clear, and thorough.	**5 points**	
-Most information presented was accurate, clear, and thorough.	**4 points**	
-Most information presented was clear but not thorough.	**3 points**	
-Information was not clear or completely accurate.	**2 points**	_____
-Every major point was well supported with relevant facts.	**5 points**	
-Every major point was adequately supported with relevant facts.	**4 points**	
-Most of the major points were supported with relevant facts.	**3 points**	
-Every point was not supported.	**2 points**	_____
-Team consistently used gestures, eye-contact and a level of enthusiasm that kept the audience's attention.	**5 points**	
-Team usually used gestures, eye-contact and a level of enthusiasm that kept the audience's attention.	**4 points**	
-Team sometimes used gestures, eye-contact and a level of enthusiasm that kept the audience's attention.	**3 points**	
-Team did not keep the audience's attention.	**2 points**	_____
-All arguments were tied to an idea and well organized.	**5 points**	
-Most arguments were tied to an idea and well organized.	**4 points**	
-All arguments were tied to an idea but not well organized.	**3 points**	
-Arguments were not tied to an idea or well organized.	**2 points**	_____
-All counter-arguments were accurate and relevant.	**5 points**	
-Most counter-arguments were accurate and relevant.	**4 points**	
-Some counter-arguments were accurate and relevant.	**3 points**	
- Counter-arguments were not accurate and/or relevant.	**2 points**	_____
		_____
Total Points		

Figure 7. *Suggested evaluation sheet for the classroom debate activity. Grades based upon point totals are entirely up to the classroom instructor*

Activity 4

Students should write a reflection paper on one or more of the following questions.

1. How do you think Gene's brother feels?
2. What if the embryo that eventually became Gene had not been selected? Discuss the ethical considerations of the embryos that were either frozen or discarded.
3. If you had Fanconi Anemia or a similar illness would you want your parents to create a sibling to be a donor?
4. If your child were ill, would you create another child to be a donor? Why or why not?

Activity 5

Divide the class into groups of four to ten students. Each group will present a skit about how Gene was told he was a "designer baby". Each group should create the characters and dialogue they find necessary for the scene. Each skit should be five to ten minutes in length.

CONCLUSIONS

The activities listed above were a challenge on two different fronts. First, it was a challenge for a non-majors bioethics class to accomplish the necessary research and complete the case study that was presented in this article. Second, it was a challenge for the freshmen, nursing students in the general biology course to engage in some of the listed activities. There were approximately 80 nursing students in the course. These students were divided into 4 different laboratory sections. Each laboratory section was assigned a different activity from those listed above.

It was interesting to see the diversity of the groups that were surveyed for Activity 1. They included health field professionals, family members, and even church members. Their findings varied depending on the group that was being surveyed.

The most revealing assignment was the students' responses to the questions listed in Activity 4, especially to question 1. "How do you think Gene's brother feels?" The students were not the least bit inhibited to share their feelings in answering this question. Their writings revealed a depth as well as a wide range of thought.

As an instructor, this case study was a great opportunity to expose non-majors to bioethics while also providing some valuable learning activities for the nursing majors. Hopefully both groups will have a better understanding of bioethics in their future endeavors.

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